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## REVIEW ARTICLE

## Staging laparoscopy for cholangiocarcinoma

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The precise role of laparoscopic assessment of biliary tract malignancy is yet to be defined. The evidence for its use has been reviewed to establish the role of laparoscopy for preoperative staging of cholangiocarcinoma. Published papers were reviewed for the evidence relevant to intrahepatic, proximal intrahepatic and distal biliary carcinoma. There is no randomized trial evaluating staging laparoscopy or laparoscopic ultrasound in the assessment of cholangiocarcinoma and the quality of the available data is extremely variable. There is a need for further studies to determine the specific role of laparoscopic staging of cholangiocarcinoma. The current standard of management should be to perform laparoscopic staging prior to proceeding to resection for patients with cholangiocarcinoma as it may prevent unnecessary laparotomy in up to 30% of patients. However, a selective approach identifying high-risk patients who will not benefit from surgical palliation may be more cost effective and future studies should be performed to identify such patients.

**Introduction**

Cholangiocarcinoma is an uncommon malignancy with an incidence of between 2 and 6 in 100,000 in Europe [1]. The tumor may present as intrahepatic (IHC), proximal extrahepatic (HC), or distal (DC), and may be multifocal. Consequently, this variation in tumor location may impact directly on its presentation, investigation, and subsequent management.

Although surgery offers the only potential cure for patients with localized disease, it is associated with significant potential morbidity and mortality. This, combined with the fact that the majority of patients will have limited life expectancy associated with advanced disease (for which resectional surgery is inappropriate), mandates accurate preoperative staging to prevent unnecessary morbidity.

While improved non-invasive imaging has resulted in accurate staging for many HPB malignancies, evaluation of cholangiocarcinoma remains a challenge.

Computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (US) form the mainstays of staging for cholangiocarcinoma. Unfortunately, and despite the introduction of newer imaging modalities such as positive emission tomo-

graphy (PET), they remain relatively poor at determining the presence of peritoneal disease and all have limitations in terms of local staging. Staging laparoscopy (SL) is a quick, safe but invasive investigation by which to determine the presence of peritoneal disease and occult dissemination within the liver. The addition of direct contact laparoscopic ultrasonography (LUS) provides the ability to assess further the local stage of the disease and to evaluate the liver for metastases. Although SL with or without LUS is widely used for many hepatobiliary and pancreatic malignancies, the indications for cholangiocarcinoma are less well defined. The aim of this article is to review the evidence for the role of SL±LUS for preoperative staging of cholangiocarcinoma (Table I).

**Literature review***Intrahepatic (IHC)*

Few studies have addressed the role of SL±LUS in the preoperative assessment of IHC specifically. Ohtsuka et al. [2] reviewed 62 patients with IHC, 14 (23%) of whom were shown to have extensive peritoneal, liver, and lymph node metastasis at the time of laparotomy. These data suggest that an

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Table I. Summary of studies assessing the efficacy of laparoscopy (SL) and laparoscopic ultrasonography (LUS) in cholangiocarcinoma based on location.

Reference	No. of patients	IHC/HC/DC	+SL	+LUS	Efficacy
3	31	11-IHC 20-HC	5	n/a	IHC- 36% HC- 25%
4	56	56-HC	14	0	25% SL
6	84	84-HC	20	14	24% SL 41.5% SL+LUS
7	23	23-DC	2	2	9% SL 12% SL+LUS

IHC =intrahepatic cholangiocarcinoma; HC =proximal extrahepatic cholangiocarcinoma; DC =distal cholangiocarcinoma.

equivalent number of unnecessary laparotomies could have been avoided had laparoscopic staging been employed. However, a small series from Goere et al. [3] demonstrated a false-negative rate with this approach. In their review of 11 patients with IHC, 4 had metastasis at laparoscopy. Of the remaining 7 patients who proceeded to laparotomy, only 4 underwent resection. One patient was found to have peritoneal metastasis at laparotomy, and 2 had vascular involvement or distant LN spread. Potentially, the yield could have been improved with the addition of LUS.

#### *Proximal extrahepatic (HC)*

In the Beaujon study [3], 20 patients with potentially resectable HC underwent laparoscopy. Five patients had disseminated disease at laparoscopy, but of the 15 who proceeded to laparotomy only 5 ultimately underwent resection. Again, the addition of LUS may have further reduced the burden of unnecessary laparotomy.

In a larger study from the Sloan Kettering Cancer Center, Weber and colleagues [4] described the use of SL in potentially resectable HC in 56 patients, 14 of whom were found to have metastatic disease at SL. Of the remaining 42 patients who went on to laparotomy, 19 had unresectable disease. Ten of these 19 patients were shown to have locally advanced disease, while 4 had peritoneal or liver metastasis. Interestingly, for patients with T1 disease, 2 of 23 (9%) patients were deemed to have unresectable disease by SL alone, while 7 patients were found to have unresectable tumors at laparotomy. For T2 disease, 11 of 29 (38%) patients had unresectable tumors at SL and 22 tumors were unresectable at laparotomy. For T3 tumors, one of four (25%) patients were shown to have unresectable tumors at SL, but all remaining patients proceeding to laparotomy had unresectable disease [5]. The authors concluded that SL should be used for all patients with T2/T3 tumors, since this provided the greatest yield with the least morbidity to the patient, although it was unclear from this study whether stage had been determined solely on radiological assessment before

laparoscopy or laparotomy. Of interest, the authors also performed LUS in 23 patients in their study; however, they did not find any patient with unresectable disease based on this investigation alone. It is therefore uncertain whether more patients undergoing LUS in this study population would have reduced the number of unnecessary laparotomies in the unresectable group in all stages.

In 2005, our own group [6] published an 11-year experience (1992–2003) using both SL and LUS in patients with suspected HC. During that time period, of the 235 patients referred for assessment, 122 were felt to be irresectable following contemporary radiological imaging. Eighty-four of the remaining 113 patients underwent laparoscopic assessment, 20 of whom were deemed unresectable by SL alone (15 with peritoneal disease and 5 with microscopically verified nodal disease outside the field of resection). With the addition of LUS, a further 14 patients were identified as having unresectable disease. One had an intra-parenchymal liver metastasis not visualized on SL and 13 due to locally advanced disease precluding resection. Based on preoperative tumor stage using the same staging system as the Memorial Sloan Kettering group [5], 14 of 19 (74%) patients with T1 disease, 25 of 40 (63%) patients with T2 disease, and 5 of 16 (31%) patients with T3 disease were thought to have resectable tumors following laparoscopic assessment. Ultimately, at laparotomy, only 8, 11, and 1 of the patients with T1, T2, or T3 disease, respectively, underwent resection. The reason for unresectability differed by MSKCC stage [5]. For those with T1 or T2 disease, 22 of the 32 (69%) patients had unresectable tumor due to metastatic disease, while for T3 disease only 4 of 15 (27%) patients had metastatic disease ( $p=0.007$ ). The yield from SL and LUS for HC was 42% with an overall accuracy of 53%. Although these figures appear higher than those of Weber and colleagues, there are a number of important issues that require consideration. First, the Edinburgh study was performed over a longer time period during which the quality of imaging undoubtedly varied and, second, a selective approach to laparoscopic assessment was employed by the authors. These studies highlight that although SL

and LUS have an apparent role to play in the staging algorithm of HC, accurate assessment of locally advanced disease remains challenging. It may be possible to employ a selective approach based both on the radiological staging and on the method of palliation most likely to be employed in the event of non-resectable disease.

#### *Distal (DC)*

Vollmer et al. [7] studied 23 patients with DC employing both SL and LUS. Two patients were found to have unresectable disease by SL alone (both due to hepatic metastases). Of the 17 patients that proceeded to LUS, 2 were deemed to have unresectable tumor due to arterial involvement. The remaining 19 patients were thought to have technically resectable tumors by combined SL and LUS assessment. Of the 16 that proceeded subsequently to laparotomy, 3 tumors were found to be unresectable, 2 had associated distant lymph node involvement, and 1 had related peritoneal and liver metastases not identified at SL and LUS.

### **Technique**

#### *Laparoscopy*

Using two 10-mm ports (one infra-umbilical and one in the right mid-quadrant), pneumoperitoneum is established. A 30-degree scope is placed and inspection of the peritoneum is performed paying particular attention to the falciform ligament, liver (including the undersurface) and diaphragm, porta, and lesser omentum. By retracting the greater omentum superiorly, the small bowel and root of the mesentery can be visualized. Any suspicious lesions are biopsied [8].

#### *Laparoscopic ultrasound*

This is best performed with a high-resolution flexible tip linear array transducer. The probe should be introduced through both ports to allow imaging in two planes. Systematic scanning of the liver should start with identification of standard landmarks and of the liver parenchyma for signs of intrahepatic liver metastasis. These can appear as hyper-, iso-, or hypo-echoic lesions on imaging. Any suspicious lesions can then be biopsied using ultrasound guidance. Subsequent to this, identification of structures in the portal triad and relationship to the primary tumor (for HC or DC) is important. The portal structures are viewed by inserting the probe through the sub-umbilical port and placing it on the hepatoduodenal ligament. This will visualize the IVC posteriorly. By rotating the probe counterclockwise, the portal vein, bile duct, and hepatic artery are visualized. By withdrawing the probe, the portal vein can be followed to the

spleno-portal confluence and continued down the SMV. Vascular invasion is suggested if there is loss of tissue planes between tumor and vessels. However, too much pressure on the probe can artificially emulate tumor involvement into vessels when it has not occurred. A fixed stenosis of the vessel in more than one plane is a sign of tumor involvement. If views are not adequate due to probe contact or CO<sub>2</sub> distortion, pneumoperitoneum can be reduced or released completely and saline can be injected into the peritoneum to improve probe contact. Furthermore, a 10-mm port placed in the left side of the abdomen can allow better visualization of the intra-pancreatic bile duct and pancreatic head. The primary lesion should be assessed to determine its proximal and distal extent (particularly important for HC), radial extension (particularly arterial and venous invasion) and lymph node metastases. Lymph nodes invaded by tumor appear as hypo-echoic nodes that are less well circumscribed. Although enlarged lymph nodes may represent the presence of metastatic disease it is not specific and should be confirmed pathologically.

### **Grading of evidence**

There is no randomized trial evaluating SL or LUS in the staging of cholangiocarcinoma, and the available data are extremely variable in terms of quality. This is due to a number of factors, including the temporal improvement in non-invasive imaging, tumor characteristics, and the variable technical aspects associated with laparoscopic evaluation. While the multiple case series have shown a reduction in the number of patients undergoing unnecessary laparotomy and ultimately decreased morbidity, the data are poor at best. There is a need for further studies to determine the specific role of laparoscopic staging of cholangiocarcinoma.

### **Consensus statement**

- The current standard of management should be to perform SL and LUS prior to proceeding to resection for patients with cholangiocarcinoma, as this will prevent unnecessary laparotomy in up to 30% of patients. However, a selective approach identifying high-risk patients who will not benefit from surgical palliation may be a more cost-effective approach and future studies should be performed to identify such patients.

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